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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/524,860

02/18/2005

Takeshi Koizumi

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EXAMINER

WOOLWINE, SAMUEL C

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

05/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/524,860

Applicant(s)

KOIZUMI ET AL.

Examiner

Samuel Woolwine

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-50 is/are pending in the application.
- 4a) Of the above claim(s) 1-36, 41, 42, 45-47 and 49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37-40, 43, 44, 48 and 50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/18/2005;11/21/2005;7/11/2006.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group III, claims 37-48 and claim 50 in part, in the reply filed on 4/9/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-36, 41, 42, 45-47 and 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/9/2007. Applicant was instructed in the Office action of 3/7/2007 to elect as a species *either* a single combination of positions as recited in claims 1, 16 or 37, *or* a single particular sequence as recited in claims 10-14, 28-35 or 44-47 (see page 4, last full paragraph of the previous Office action). Applicant has elected the species SEQ ID NO: 17, recited in claim 44. An examination of SEQ ID NO: 17 reveals that this sequence corresponds to positions 133-153 of SEQ ID NO: 3. Therefore, the elected species encompasses the positions recited in claim 40, and this claim will remain pending and under consideration. Claims 41 and 42, however, recite positions that are not encompassed by the elected species, and are therefore withdrawn from further consideration since they, like claims 45-47, are drawn to non-elected species.

The requirement for restriction and election of species is made FINAL.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112—2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-40, 43, 44, 48 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite because claims 37, 38 and 48 recite nucleotide position numbers "in the gene (*recA*) encoding the RecA of SEQ ID NO: 3 in the sequence listing". It is not clear whether these position numbers are intended to refer to SEQ ID NO: 3 itself, or to any sequence "encoding the RecA". Since a sequence "encoding the RecA of SEQ ID NO: 3" may contain additional sequences either before or after the sequence disclosed in SEQ ID NO: 3, yet still encode the RecA of SEQ ID NO: 3, nucleotide position numbers become ambiguous. Because claims 39, 40, 43, 44 and 50 are dependent on claim 38, these claims are also vague and indefinite. Applicant is advised to amend the claims to simply recite "...at any of positions X, Y,...Z of SEQ ID NO: 3...". For purposes of further examination, the recited nucleotide positions will be assumed to refer exclusively to SEQ ID NO: 3.

Claim 37 is also vague and indefinite because it is unclear what is meant by the recitation "A gene fragment represented by SEQ ID NO: 3". This could be interpreted to

mean "a fragment of SEQ ID NO: 3", or "a nucleic acid sequence having similarity to SEQ ID NO: 3" (which would itself be vague and indefinite, and lacking in written description), or "a nucleic acid sequence that is capable of hybridizing to SEQ ID NO: 3" (which would also lack written description), or "any nucleic acid sequence containing one or more nucleotides at any of positions 9, 81, 138, etc of SEQ ID NO: 3" (which would read on any nucleotide sequence of 15 or more nucleotides having, for example, the nucleotide "T", which is the nucleotide found at position 153 of SEQ ID NO: 3). Note that claims 38 and 48 do not recite "containing 15 or more continuous nucleotides of SEQ ID NO: 3", but only that the claimed polynucleotide contains "15 or more continuous nucleotides" and that "one or more nucleotides are nucleotides at any of positions...in the gene...". With regard to claim 37, "Represented by" could also be interpreted to mean a nucleic acid sequence from the same genome as SEQ ID NO: 3, or a nucleic acid encoding a protein having the same biological function or activity as RecA. For purposes of examination over the prior art, the examiner will assume that "A gene fragment represented by SEQ ID NO: 3" means "a fragment of SEQ ID NO: 3".

Claims 39, 40, 43 and 50 are also vague and indefinite because claim 39 recites the limitation "wherein a region that contains, at a high frequency, a position(s) unique to *Vibrio vulnificus* as specified in claim 38 is used". The instant specification was searched for the term "frequency". Other than the claims, this term only appears in the following text: "a gene that is transmitted horizontally at a high frequency" (paragraph [0009] of the published application). The public would have no idea what Applicant considers to be "a high frequency", and therefore the metes and bounds of claim 39 are

unclear. Because claims 40, 43 and 50 depend from claim 39, these claims are also vague and indefinite. It is also noted that the limitation "wherein a region that contains, at a high frequency, a position(s) unique to *Vibrio vulnificus* as specified in claim 38 is used" is a recitation of intended use and therefore carries no patentable weight. For purposes of further examination, this limitation will not be considered to distinguish over any prior art that teaches the *structure* of the claimed primer.

Claim Rejections - 35 USC § 112—Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40, 43, 44, 48 and 50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

For claim 37, the problem stems from the limitation "A gene fragment represented by SEQ ID NO: 3". As discussed for the rejection under 35 U.S.C. 112, 2nd paragraph above, claim 37 could be interpreted simply as any nucleic acid sequence containing a nucleotide found at the recited positions in SEQ ID NO: 3 (for example, a "T" residue, which is found at position 153 of SEQ ID NO: 3). A similar interpretation can be made for claims 38 and 48, which require only that the claimed primer/probe comprises at least 15 nucleotides, and comprises a nucleotide found at the recited

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positions of SEQ ID NO: 3. Therefore, the claims define an incredibly broad genus of possible polynucleotides. As all claims depend from either claim 37, 38, or 48, all claims are likewise rejected under this section.

As stated in MPEP 2163 (II)(A)(3)(a)(ii), the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Reduction to practice:

The sequence of SEQ ID NO: 3 is disclosed, as are the sequences of SEQ ID NOS: 17-20 which are apparently derived from SEQ ID NO: 3. However, as noted above, the claims as currently written encompass a genus far beyond the disclosure of SEQ ID NO: 3. The claims read, for example, on gene fragments from genes encoding the RecA homologs from other species (since these homologous genes undoubtedly contain one or more nucleotides that are found at the recited positions of SEQ ID NO: 3). There is no written description of such homologous genes. Indeed, the claims as written structurally require, at most, a polynucleotide of at least 15 nucleotides, which contain a nucleotide found at one of the recited positions in SEQ ID NO: 3, and which could be used as a primer or probe for detecting *Vibrio vulnificus* (claims 38-40, 43, 44 and 48) or could be used to design such a primer or probe (claims 37, 50). In other

words, the claims are not limited to the sequences within the disclosed SEQ ID NO: 3.

Reduction to drawings:

There is a drawing (figure 4) depicting a sequence for recA, presumably the same as SEQ ID NO: 3.

Relevant identifying characteristics:

Applicant has disclosed the sequence of SEQ ID NO: 3, but has not identified relevant identifying characteristics of the genus encompassing any polynucleotide greater than 15 nucleotides in length, containing a nucleotide found at recited positions of SEQ ID NO: 3, that could be used as a primer or probe, or used to design a primer or probe, for quantifying, detecting or identifying *Vibrio vulnificus*. It seems that Applicant is attempting to claim fragments of the sequence of SEQ ID NO: 3 that encompass certain positions of the sequence. Applicant is advised to amend the claims so that broader claim interpretations, which result in an unintentionally large and undescribed genus, do not apply.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-40, 44 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank® GI:16565115, 1-Nov-2001, [online], [retrieved on 5/22/2007],

retrieved from the Internet: <URL:

www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?16565115:OLD12:801996>.

With regard to claim 37, GenBank® GI:16565115 discloses a nucleotide sequence of 543 nucleotides that is a “gene fragment represented by SEQ ID NO: 3”. An alignment of SEQ ID NO: 3 with GenBank® GI:16565115 is shown below. It is noted that GenBank® GI:16565115 positions 238-258 correspond exactly to positions 133-153 of SEQ ID NO: 3 (and thus also the elected species of SEQ ID NO: 17). This particular region is underscored in the alignment below. GenBank® GI:16565115 is from *Vibrio vulnificus* and can be used for designing a specific gene amplification primer or a specific probe (in fact this sequence could itself serve as a specific gene amplification primer or a specific probe).

With regard to claim 38, GenBank® GI:16565115 contains at least 15 continuous nucleotides, including nucleotides found at positions 133-153 of SEQ ID NO: 3, and can be used as a gene amplification primer.

With regard to claim 39, the limitation “wherein a region that contains, at a high frequency, a position(s) unique to *Vibrio vulnificus* as specified in claim 38 is used” is a recitation of intended use that does not structurally distinguish over the primer disclosed by GenBank® GI:16565115.

With regard to claim 40, GenBank® GI:16565115 contains at least 15 continuous nucleotides, including nucleotides found at positions 133-153 of SEQ ID NO: 3, and can be used as a gene amplification primer.

With regard to claim 44, GenBank® GI:16565115 positions 238-258 correspond exactly to positions 133-153 of SEQ ID NO: 3 (and thus also the elected species of SEQ ID NO: 17). This particular region is underscored in the alignment below. The entire sequence of GenBank® GI:16565115 can be used as a gene amplification primer, and it "contains" SEQ ID NO: 17.

With regard to claim 48, as discussed above, GenBank® GI:16565115 positions 238-258 correspond exactly to positions 133-153 of SEQ ID NO: 3. GenBank® GI:16565115 also contains 15 or more continuous nucleotides and can be used as a probe for detecting, quantifying or identifying *Vibrio vulnificus*.

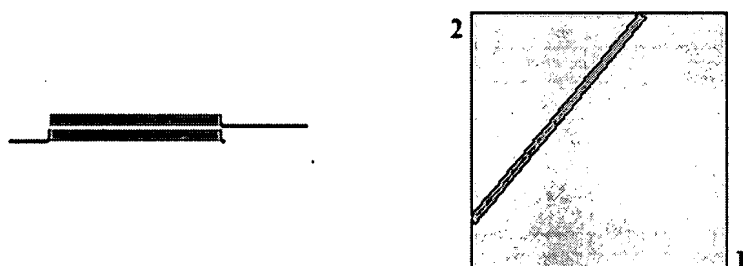
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Sequence 1: lc|SEQID NO 3

Length = 648 (1 .. 648)

Sequence 2: gi|16565115|gb|AF311535.1|Vibrio vulnificus strain 9067-96 recombinase A (recA) gene, partial cds.

Length = 543 (1 .. 543)



NOTE: Bitscore and expect value are calculated based on the size of the nr database.

NOTE: If protein translation is reversed, please repeat the search with reverse strand of the query sequence.



Score = 797 bits (402), Expect = 0.0
Identities = 404/434 (93%), Gaps = 0/434 (0%)
Strand=Plus/Plus

```
Query 1 CCAATGGGCGTATCGTTGAAATTTTTGGTCCAGAATCTTCAGGTAAAACCACGTTGACC 60
      |||
Sbjct 106 CCAATGGGCGTATCGTTGAAATTTTTGGTCCAGAATCTTCAGGTAAAACCACGTTGACC 165

Query 61 CTTGAGCTGATCGCTGCRGCTCAACGTGAAGGCAAACTTGTGCGTTTATCGATGCGYAG 120
      |||
Sbjct 166 CTTGAGCTGATCGCTGCGGCTCAACGTGAAGGCAAACTTGTGCGTTTATCGATGCCGAG 225

Query 121 CACGCGTTRGATCCTGTGTATGCGAAGAARCTTGGCGTWAATATCGACCARTTRTTGGTA 180
      |||
Sbjct 226 CACGCGTGGATCCTGTGTATGCGAAGAAGCTTGGCGTTAATATCGACCAGTTGTTGGTA 285

Query 181 TCTCAGCCYGAYACBGGTGAACAAGCRTTGGAAATCTGTGATGCKCTTGCTCGCTCAGGK 240
      |||
Sbjct 286 TCTCAGCCGACACCGGTGAACAAGCATTGAAATCTGTGATGCTCTTGCTCGCTCAGGT 345

Query 241 GCGGTTGAYGTTATTGTGTGCGAYTCTGTGCMGCATTGACRCAAAGGCAGAAATYGAA 300
      |||
Sbjct 346 GCGGTTGACGTTATTGTGTGCGACTCTGTTGCAGCATTGACACCAAAGGCAGAAATCGAA 405

Query 301 GGTGAGATGGGYGAYTCGCACATGGGCTCNCAAGCTCGTATGCTMTCTCAAGCGATGCGT 360
      |||
Sbjct 406 GGTGAGATGGGCGACTCGCACATGGGCTTCAAGCTCGTATGCTATCTCAAGCGATGCGT 465

Query 361 AAGYTAACGGGKAACCTAAARCAGTCTAACTGTATGTGTATCTTCATYAACCAGATYCGT 420
      |||
Sbjct 466 AAGTTAACGGGTAACCTAAAGCAGTCTAACTGTATGTGTATCTTCATCAACCAGATCCGT 525

Query 421 ATGAAGATYGGKGT 434
      |||
Sbjct 526 ATGAAGATTGGTGT 539
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Claims 37-40, 43, 44, 48 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Random Primer 24, sold by New England Biolabs (see page 121 of the 1998/99 New England Biolabs Catalog; this reference was cited and supplied in the previous Office action).

Random Primer 24 contains every possible 24-nucleotide sequence. The following calculations rely on facts provided on page 284 of the catalog, specifically the mass of 1.0 A_{260} unit of single-stranded DNA and the molecular weight of single-stranded DNA per nucleotide (i.e. half the weight of a double-stranded DNA per basepair):

Random 24-mer:

Molecular weight of 24-mer:

$$24 \times 325 \text{ daltons/nucleotide} = 7,800 \text{ daltons} = 7,800 \text{ g/mol}$$

Number of possible 24-mers:

$$4^{24} = 2.8 \times 10^{14} \text{ molecules}$$

How many molecules of 24-mer in a vial sold by NEB:

$$1 A_{260} \text{ unit} = 33 \mu\text{g} = 3.3 \times 10^{-5} \text{ g}$$

$$3.3 \times 10^{-5} \text{ g} \div 7,800 \text{ g/mol} = 4.2 \times 10^{-9} \text{ mol}$$

$$(4.2 \times 10^{-9} \text{ mol}) \times (6.02 \times 10^{23} \text{ molecules/mol}) = 2.5 \times 10^{15} \text{ molecules}$$

How many vials needed to sum to 1 of each possible 24-mer:

$$2.8 \times 10^{14} \text{ molecules} \div 2.5 \times 10^{15} \text{ molecules} = 0.11 \text{ vial}$$

Put another way, every vial of Random Primer 24 sold by New England Biolabs would be expected to contain 9 copies of every possible 24-nucleotide sequence. Therefore, Random Primer 24 would contain every possible gene fragment imaginable that is 24 nucleotides in length, thus meeting the limitations of claims 37-40, 43, 44 and

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48, including the limitation of "at least 15 continuous nucleotides" recited in claims 38 and 48. Furthermore, with regard to claim 50, Random Primer 24 is itself a kit (it was a commercially sold product at least as early as 1998). It could also be used for detecting, quantifying or identifying *Vibrio vulnificus*. For example, it could be used to make a labeled probe by random priming using a *Vibrio vulnificus* template nucleic acid.

Conclusion

No claims are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Young J. Kim/
Primary Examiner
Art Unit 1637
Technology Center 1600

A handwritten signature in cursive script, appearing to read 'S. Woolwine', is written in black ink.